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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,316	02/09/2005	Nicholas Peter Franks	YOUZ 2 00109	6458

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,316	FRANKS ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,6,8 and 11-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,6,8 and 11-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/14/08 has been entered.

Claims 1, 4, 7, 9 and 10 have been cancelled. Claims 2, 3, 5, 6, 8 and 11-24 are pending and under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 7/14/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 6, 11-13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukura et al. (Prog. Neuro-Psychopharmacol. & Biol Psychiat. 2000, 24, 1357-1368).

Fukura et al. disclose treatment of pregnant rats and neonatal rats with anesthetic xenon gas mixture (70% xenon 30% oxygen) (Abstract and Page 1359, Exposure to Anesthetic gases). Fukura et al. specifically examined the effect of xenon on the fetal rat brain thus anticipating instant claims 2, 6, 11 and 12 (Page 1359, Preparation of isolated growth cone Particles). Oxygen is a diluent thus anticipating instant claims 13 and 17. Fukura conclude that xenon is safe for perinatal neuronal development (Abstract).

Response to arguments:

Applicant asserts that the patient population in Fukura is not in need of analgesia and therefore the claim is not anticipated. Respectfully, the Examiner cannot agree. Fukura et al. clearly disclose preparing ICG from fetal and neonatal rat forebrains (page 1359, preparation of Isolated Growth Cone Particles). The fetal and neonatal rats were ***in need of analgesia*** before having their brains homogenized. Clearly, a subject about to have their brains homogenized is in need of analgesia.

Claim Rejections - 35 USC § 102

Claims 12, 17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Lane et al. Science 1980, 210(4472), 899-901).

Lane et al. disclose treating pregnant Spraque-Dawley rats with 70-75% v/v xenon and oxygen gas mixture and examined 160 fetuses (Page 900, Table 1 group D and right column). Oxygen is a diluent/carrier. It is the Examiner's position that the rat fetuses received any beneficial analgesic effect of the xenon gas mixture administered to the parent.

Response to arguments:

Applicant asserts that there is no disclosure of administering xenon to the mother of a fetal subject where the fetal subject is ***in need of analgesia***. Respectfully, the Examiner cannot agree for the following reason. Lane et al. examined macroscopic organ anomalies in the fetal rats (page 900, right column). Therefore, the fetal rats about to be experimented upon were ***in need of analgesia*** before undergoing these procedures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 3, 5, 6, 8 and 11-24 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukura et al. (Prog. Neuro-Psychopharmacol. & Biol Psychiat. 2000, 24, 1357-1368) in view of Georgieff (US 6,197,323) and Fishman (US 5,099,834) and Ohashi et al. Anesthesiology 2002, 96, A1291 and with respect to claims 5 and 24, Franks et al. (US 6,274,633).

Applicant claims a method of providing analgesia in a newborn and in a fetal subject comprising administering a therapeutically effective amount of xenon.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The references of Fukura et al. are described in detail above and those discussions are hereby incorporated by reference.

Georgieff teaches liquid anesthetic lipophilic gas preparations and methods of inducing analgesia comprising xenon and in a fatty emulsion (excipient/carrier) that can be administered intravenously or by inhalation (Abstact; column 9, lines 10-16; column 10, lines 22-65 and claims 16). Georgieff teach ointments and creams which can be applied to the damaged tissue thus reading on transdermal application (column 9, lines 40-54).

Fishman teaches administration of xenon gas mixtures, from 60 to 78.5 mole percent xenon, to women of childbearing age (Abstract and claims 1-14). Fishman teaches that nitrous oxide is toxic to a fetus (column 1, lines 49-60).

Franks et al. teach methods of relieving neuropathic pain comprising administering xenon to a mammal in need thereof (Claims 1 and 3). The method further comprises administering an anaesthetic or sedative agent that promotes GABAergic activity (claim 8).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. Fukura et al. do not expressly teach a 20 to70 % v/v xenon/air mixture; administration of xenon in the form of a lipid emulsion or where xenon is administered intravenously, neuraxially or transdermally. These deficiencies in Fukura et al. are cured by the teachings of Georgiefff, and Fishman.

2. Fukura et al. do not expressly teach adding an anesthetic agent that promotes GABAergic activity or other analgesics. This deficiency in Fukura et al. is cured by the teachings of Franks et al.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a xenon gas mixture of 20 to 70% v/v xenon air, or administer the xenon in the form of lipid emulsion intravenously, as suggested by Georgieff, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because it is mere routine optimization of the gas mixture as taught by Fukura et al. Applicant has not shown the criticality of using 20% oxygen and 70% xenon. The active is xenon and the art teaches using 70% xenon. Oxygen is simply a carrier. One of ordinary skill in the art would recognize other means of providing analgesia to a patient such as intravenous administration of xenon in a carrier as taught by Georgeiff. One of ordinary skill in the art would be motivated to use xenon, in such alternative forms in addition to inhalation, because nitrous oxide is taught by Fishman to be toxic

to a fetus. So, one of ordinary skill in the art would be motivated to administer a therapeutically effective amount of xenon to women of childbearing age. The route of administration is easily determined by one of ordinary skill in the art. The fetus would intrinsically benefit from any analgesic properties of the gas.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add an anesthetic that promotes GABAergic activity, as suggested by Franks et al., in the method of Fukura et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Franks et al. teach the combination of xenon with other anesthetics and analgesics such as opiates or NSAIDS because these agents are directed toward relief from pain. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant asserts that the cited references do not describe administering xenon to a newborn or fetal subject ***in need of analgesia***. Respectfully, the Examiner cannot agree. As explained above the subjects were in need of analgesia. The 1.132 Declaration by Dr. Aubrey Maze unmistakably states that: "sub-population are those newborns or fetuses that will experience stress or pain sufficient to necessitate analgesia such as those that will undergo certain surgical procedures…" (bullet point 6 of the Declaration). Clearly, a clinical Professor of Anesthesiology supports administration of xenon to patients about to undergo surgical procedures which would include the experimental surgical procedures performed on the subjects cited above. Regarding the list of procedures in bullet point 7 of the declaration, this is not an exhaustive list as evidenced by the term "such as". The declaration is insufficient to overcome the rejection of record.

Applicant's arguments are not persuasive and the Examiner maintains the rejections

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/

Examiner, Art Unit 1616